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LETTER TO THE EDITOR
Successful Handling of Autoimmunity in X-linked Thrombocytopenia (XLT) Using Mycophenolate Mofetil

To the Editor: A 12-year-old male, the only child of a non-consanguineous Portuguese couple, was admitted in a tertiary pediatric hospital in Lisbon because of severe auto-immune hemolytic anemia (minimum value of hemoglobin 4.3 g/dl), with strongly positive direct IgG Coombs test. He had a personal history of mild eczema and a previous diagnosis of chronic immune thrombocytopenic purpura (ITP), with persistently positive titers for anti-platelet antibodies. The ITP had been resistant to intravenous immunoglobulin G (IGIV) and was partially controlled (platelet count over 50,000/μl) with corticosteroids (prednisolone 2 mg/kg/day), despite two hospital admissions for severe, uncontrolled thrombocytopenia.

During hospitalization the patient had severe hemolysis for 14 days despite the infusion of IVIG and the administration of pulses of corticosteroids (30 mg/kg of methylprednisolone for 5 days), needing the transfusion of two units of packed red cells. The platelet count was normal at admission but decreased gradually to a minimum value of 25,000/μl, with normal mean platelet volume (9 fl). He was discharged from the Hospital after 27 days of hospitalization, on 1.5 mg/kg/day of prednisolone. As outpatient he had a severe relapse with bicytopenia (hemoglobin 8 g/dl, platelets 20,000/μl) as prednisolone was weaned (at the dose of 0.8 mg/kg/day), needing higher doses of steroids.

In the presence of a refractory Evans syndrome in an adolescent with mild eczema, after excluding common causes of chronic ITP, such as systemic lupus erythematosus, auto-immune lymphoproliferative syndrome (ALPS), common variable immunodeficiency or HIV, direct sequencing of the WASP gene was performed, revealing a missense mutation c.1378C>T (p.Pro460Ser) in exon 11. This mutation had previously been described as causing X-linked thrombocytopenia [1]. This patient had a score of 5 in the WAS scoring system [2] (autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura), contradicting the classical benignity attributed to XLT (scores 2 and 3) [3].

Due to the severity of the disease and the lack of control with high and prolonged doses of corticosteroids, treatment with mycophenolate mofetil (MMF) 300 mg/m^2 twice a day was proposed. This was based on the excellent results previously reported of its utilization in patients with immune dysregulation and Evans syndrome, namely in ALPS with more than 30 patients treated, 80% of whom with prompt resolution of auto-immunity [4] and well tolerated adverse events [5].

Mycophenolate mofetil (MMF) is a prodrug of mycophenolic acid (MPA), an inhibitor of inosine monophosphate dehydrogenase. MPA depletes guanosine nucleotides preferentially in T and B lymphocytes and inhibits their proliferation, thereby suppressing cell-mediated immune responses and antibody formation. MPA also inhibits the glycosylation and expression of adhesion molecules, and the recruitment of lymphocytes and monocytes into sites of inflammation and finally, it decreases the production of nitric oxide, which contributes to its anti-inflammatory activity [6].

Within 4 weeks of starting MMF, we were able to stop the corticosteroids, with complete resolution of the cytopenias. After 12 months of follow-up, the patient maintains a normal platelet count and hemoglobin, with no relapses while receiving immunosuppressive therapy with MMF.

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